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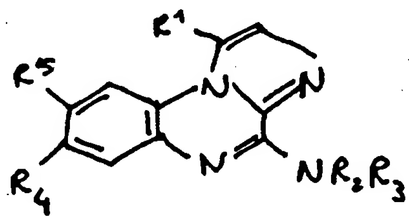

(I)

(57) Abstract

There are described imidazo[1,2-a]quinoxalin-4-amines derivatives of formula (I) and salt thereof active as adenosine antagonists and a process for their preparation and pharmaceutical compositions containing them as therapeutically active compounds for psychiatric and neurological disorders of the central nervous system.

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IMIDAZO[1,2-a]QUINOXALIN-4-AMINES ACTIVE AS ADENOSINE ANTAGONISTS, PROCESS FOR THEIR PREPARATION AND PHARMACEUTICAL COMPOSITIONS THEREOF.

DESCRIPTION

The present invention relates to the imidazo[1,2-a]quinoxalin-4-amines and their salts, that are active as antagonists of the adenosine receptors; a process for their preparation as well as the pharmaceutical compositions containing them as active ingredients that are useful in the theraphy for the treatment of various psychiatric and neurological disorders of the central nervous system.

It is known that theophylline (1,3-dimethylxanthine) and caffeine (1,3,7-trimethylxanthine) are capable of antagonizing the effects of adenosine through interaction with its receptors, and that it is mainly to such a property that their central nervous system stimulant effects are to be ascribed. However the presence of pharmacologically relevant effects also at the heart, kidney and smooth muscle level has determined a serious limitation to the therapeutical use of these substances as agents for effectively treating the central nervous system diseases characterized by abnormalities in the neuronal transmission processes, such as, for example, depression and senile dementia. Moreover, their low affinity to the adenosine receptors implies that the therapeutically effective dosages are too close to those causing serious side effects at the central level too.

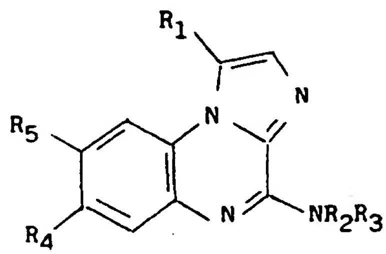
A series of compounds having various non-xanthine structures have exhibited, at different levels, affinity to the adenosine receptors (see for example documents EP 515,107 A2 and *J. Med. Chem.* 1991, 34, 1202), but none of them has the structure of imidazo[1,2-a]quinoxalin-4-amines.

Several derivatives of imidazo[1,2-a]quinoxaline derivatives have been described in the literature: for example in U.S. Patent N. 5,182,386 imidazoquinoxalinones are disclosed that interact with the central GABA receptors, whilst in WO 94/22865 analogous compounds (especially derivatives of 4,5-dihydro-4-oxoimidazo [1,2-a]quinoxaline-2-carboxylic acid) are described as antagonists of excitatory amino acids. In no case, however, an affinity of such substances to the adenosine receptors has been pointed out.

With the present invention, it has surprisingly been discovered that a group of imidazo[1,2-a]quinoxalin-4-amines are potent antagonists of the adenosine receptors that are active *in vivo* on the central nervous system at much lower dosages as compared with the compounds that are presently in general use in theraphy.

The compounds of the invention might therefore exhibit a lower incidence of side effects, especially at the peripheral level.

The present invention relates therefore to a compound of the formula (I):



(I)

wherein:

R_1 is hydrogen or methyl;

R_2 is hydrogen, straight- or branched- chain (C_1-C_6)alkyl;

R_3 is hydrogen, straight- or branched- chain (C_1-C_8)alkyl that is possibly substituted with OH, (C_3-C_8)cycloalkyl;

or R_2 and R_3 together form

```
------(CH2)m
            \
             Z
            /
------(CH2)n
```

wherein Z is a direct bond, or O, NR_6, R_6 being a straight- or branched- chain (C_1-C_6)alkyl;

m and *n*, same or different, are 1, 2 or 3;

R_4 and R_5 can be the same or different and are hydrogen or halogen chosen from Cl, F, Br;

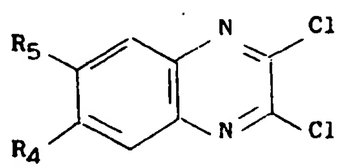
and its pharmacologically acceptable salts;

In the present invention, there are preferred the compounds of formula (I) in which R_1 is hydrogen or methyl, R_2 is hydrogen, R_3 is hydrogen, straight- or branched- chain (C_1-C_6)alkyl that is possibly substituted with OH, (C_5-C_6)cycloalkyl, R_4 and R_5 can be the same or different and are hydrogen, chlorine or fluorine.

Especially preferred is the compound of formula (I) in which R_1 is methyl, R_2 is hydrogen, R_3 is cyclopentyl, R_4 and R_5 are both hydrogen, that is the compound 4-cyclopentylamino-1-methylimidazo[1,2-a]quinoxaline.

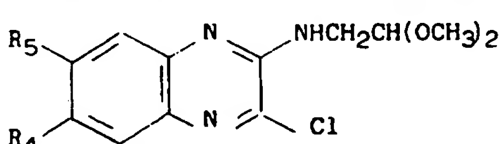
The salts of the compounds of formula (I) comprise the acid addition salts that can be prepared *in situ* during the final isolation and the purification or by means of a separate reaction of the free base with the suitable organic or inorganic acid chosen, for example, from hydrochloric, hydrobromic, phosphoric, metha-phosphoric, nitric, sulphuric, tartaric, acetic, citric, malic, lactic, fumaric, benzoic, glycolic, gluconic, succinic and p-toluene sulfonic acids.

An object of the present invention is also a process for the preparation of the compounds of the general formula (I). Said process comprises reacting the 2,3-dichloroquinoxaline of the formula (II)

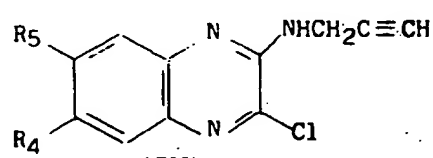


(II)

wherein R4 and R5 are as defined for the compound of formula (I), with amino acetaldehyde dimethyl acetal or with propargyl amine, thereby to obtain, respectively, the compounds of the formulae (III) and (IV)

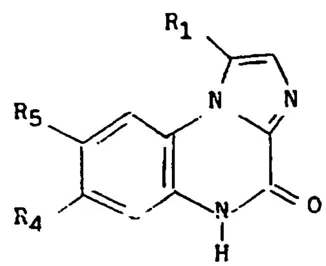


(III)



(IV)

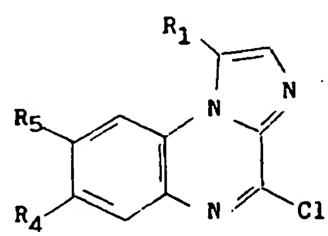
that are subsequently submitted to a cyclization reaction in an acidic medium, preferably at a temperature comprised between 50 and 120°C, to obtain the imidazo[1,2-a]quinoxalin-4(5H)-ones of formula (V)



(V)

in which R_1 is hydrogen or methyl depending on whether the starting compound was compound (III) or compound (IV), respectively, R_4 and R_5 being as defined above.

The transformation of the compounds of formula (V) into the inventive compounds having the formula (I) can be carried out following two different synthetic sequences: in the first one, the chloride of the formula (VI)



(VI)

in which all the substituents are as already defined, said chloride being obtained by treatment of compound of formula (V) with $POCl_3$ or another chlorinating agent, is reacted with the suitable amine HNR_2R_3, in which R_2 is hydrogen, straight- or branched- chain (C_1-C_4)alkyl; R_3 is

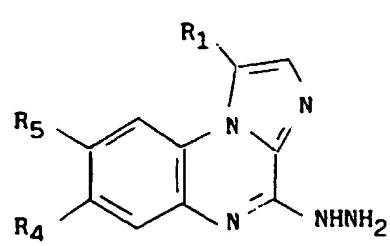
hydrogen, straight or branched chain (C_1-C_6)alkyl, possibly substituted with hydroxy, (C_3-C_6)cycloalkyl; or R_2 and R_3 together form

```
-------(CH2)m
             \
              Z
             /
-------(CH2)n
```

wherein Z is a direct bond, or O, NR_4, R_4 being a straight- or branched- chain (C_1-C_6)alkyl; *m* and *n*, same or different, are 1, 2 or 3.

As an alternative, the compound of formula (V) can be directly converted into the compounds of formula (I), by reacting it with a silylating agent, such as hexamethyl disilazane and the suitable amine HNR_2R_3 in which R_2 and R_3 are as defined in formula (I), at a temperature between 80 and 180°C, possibly in the presence of a catalyst, such as ammonium sulphate.

The preparation of the compounds of formula (I) in which R_2 and R_3 are both hydrogen, can also be carried out by reacting the chloride of formula (VI) with hydrazine to obtain a compound of formula (VII)



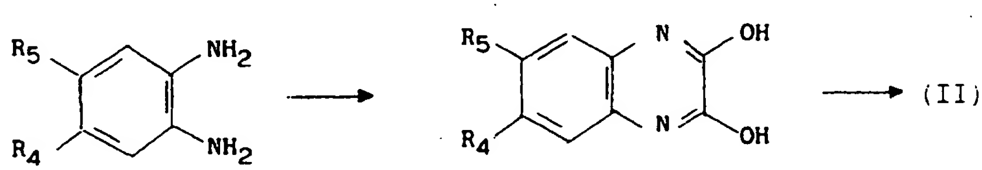
(VII)

in which all the substituents are as defined above, followed by hydrogenation of this compound by conventional methods, such as, for example, hydrogen and palladium-on-carbon, or Raney nickel.

The preferred compound of the present invention can be prepared according to the general process described above through the formation of the compound of formula (V). Said compound is then converted to the preferred compounds of formula (I) by means of either synthetic sequence shown above. For example, the especially preferred compound of formula (I) of the present invention can be prepared by treating 2,3-dichloroquinoxaline (compound of formula (II) in which R_4 and R_5 are both hydrogen) with propargylamine to obtain the 2-propargylamino-3-chloroquinoxaline (compound of formula (IV) in which both R_4 and R_5 are hydrogen), followed by reacting this latter compound in an acidic medium, for example with concentrated sulphuric acid, at a temperature of between 50 and 120°C, to give 1-methylimidazo[1,2-a]quinoxalin-4(5H)-one (compound of formula (V) in which R_1 is methyl and R_4 and R_5 are both hydrogen). This compound can finally be converted to 4-cyclopentylamino-1-methylimidazo[1,2-a]quinoxaline through the formation of the intermediate 4-chloro-1-methylimidazo[1,2-a]quinoxaline (compound of formula (VI) in which R_1 is methyl and R_4 and R_5 are both hydrogen) by chlorination with one of known chlorinating agents at a temperature of between 50 and 150°C, followed by the reaction of the latter compound with cyclopentylamine, or

alternatively, by reaction of 1-methylimidazo[1,2-a]quinoxalin-4(5H)-one with cyclopentylamine in hexamethyl disilazane or other silylating agent at a temperature of between 80 and 180°C, possibly in the presence of a catalyst, such as ammonium sulphate.

The preparation of the compounds of formula (II), when they are not commercially available, can be carried out with methods such as the one shown below. Specifically, phenylenediamine (VIII) is reacted with dialkyl oxalate to give the 2,3-dihydroxyquinoxaline (IX), wich is then subjected to a chlorinating reaction with one of the usual chlorinating agents, such as for example $POCl_3$, thereby obtaining the compounds (II)



(VIII) (IX)

As shown hereinafter in Examples 26 to 30, the compounds of formula (I) of the present invention are antagonists of the adenosine receptors, are active on the central nervous system and can therefore be advantageously used as active ingredients for the preparation of medicaments that are useful in therapy for the treatment of various psychiatric disorders of the central nervous system, such as the depressive syndromes of various etiology and symptomatology and mood disorders in general, bulimia nervosa, sleep disorders, obsessive-

compulsive disorders, phobias, panic attacks. Further indications are neurological diseases, such as pre-senile and senile dementia, the Alzheimer's disease, the multiinfarctual dementias, the encephalopathies of toxic or traumatic origin, the Parkinson disease, the post-neurological deficits, the respiratory depression, the neonatal cerebral damage.

Besides being employed as drugs acting on the central nervous system, the compounds of the present invention and their salts could be used for the treatment of diseases of the renal system, such as acute renal failure, or of diseases of the cardiovascular system.

For all the above-mentioned therapeutical uses, the compounds of the present invention can be administered by oral, transdermal or transmucosal route, parenterally or rectally in formulations containing them as the active ingredients at a therapeutically effective dosage with conventional, non-toxic pharmaceutical excipients. The term parenteral as used herein comprises subcutaneous, intravenous, intramuscolar and intracerebroventricular injections. If the compounds of the present invention are in the form of a pharmaceutical composition, as in a preferred embodiment of the invention, the precise formulation employed will obviously depend on the administration route chosen.

The pharmaceutical compositions that are suitable for the oral administration can be for example tablets, aqueous or oily suspensions, dispersible powders or granules, hard or soft capsules, syrups or elixirs. The

compositions for the oral administration can contain one or more sweetening agents, colorants, flavouring and preserving agents that are suitable to make the pharmaceutical composition elegant and palatable.

The formulations for oral administration comprise tablets in which the active ingredient is admixed with non-toxic, pharmaceutically acceptable excipients. Said excipients can be inert diluents, such as calcium carbonate, sodium carbonate, lactose, calcium phosphate or sodium phosphate; granulating or disgregating agents, such as wheat starch or alginic acid; binding agents, such as starch or gelatines; lubricant agents, such as magnesium stearate, stearic acid or talc.

The tablets can be non-coated or coated with conventional techniques known to a person skilled in the art in order to delay disintegration and absorption in the gastrointestinal tract, in order to achieve a sustained release action.

The aqueous suspensions generally contain the active ingredients admixed with the suitable excipients. The excipients can be suspending agents, such as sodium carboxymethyl cellulose, methyl cellulose, hydroxypropyl methyl cellulose, sodium alginate, polyvinylpyrrolidone; dispersants and wetting agents. They can also contain one or more preservatives, such as ethyl and n-propyl p-hydroxybenzoate; one or more flavouring agent; one or more sweetening agents.

The oily suspensions can be formulated by suspending the active ingredient in a vegetable or

mineral oil; they can contain sweetening agents and flavouring agents in order to make the preparation palatable.

The dispersible powders and granules that are suitable to the preparation of an aqueous suspension by adding water contain the active ingredient in admixture with the dispersing or wetting agent, a suspending agent and one or more preserving agents.

The pharmaceutical compositions of the present invention can also be in the form of a water/oil emulsion. The oily phase can consist of a vegetable or mineral oil. The emulsifying agents can be natural gums, such as acacia, or natural phosphatides, such as lecithins, or natural or synthetic fatty acid esters. The syrups and the elixirs can be formulated with sweetening agents, for example glycerol, sorbitol or sucrose.

The pharmaceutical compositions can be in the form of aqueous or oily, sterile injectable suspensions. The suspensions can be formulated with the known techniques by using dispersing or wetting agents and suspending agents that are known in the art. The sterile injectable preparations can be sterile injectable solutions or suspensions in a non-toxic solvent or diluent that is suitable for the parenteral use.

The compounds of the present invention can also be administered by the rectal route in the form of suppositories. These compositions can be prepared by mixing the active ingredient with a suitable, non irritating excipient that is solid at room temperature

but liquid at the rectal temperature, thereby melting in rectum to release the drug. The polyethylene glycols and the cocoa butter are suitable compounds for this purpose.

The therapeutically or prophylactically effective amounts of a compound of the present invention will depend on a number of factors including, for example, the age and weight of the patient, the severity of the specific disease requiring the treatment, the administration route. However, an effective amount of the compound of the present invention for the treatment of depressive syndromes and of senile dementia will generally be comprised in the range of 0.005-20 mg/kg of body weight per day, more frequently in the range of 0.05-2 mg/kg per day.

In order to better illustrate the present invention, the following examples are reported, that are in no way to be considered as limiting.

<u>Example 1</u>

(a) A mixture of 5.0 g of 2,3-dichloroquinoxaline and 5.5 ml of aminoacetaldehyde dimethyl acetal in 75 ml of ethanol is refluxed for 4 h. After concentrating under vacuum, the resulting mixture is added with water and extracted with ethyl acetate. The organic extracts are then washed with saturated NaCl, dried and evaporated. The residue is finally chromatographed on SiO (eluent: CH_2Cl_2), thereby obtaining 5.0 g of 2-chloro-3-(2,2-dimethoxyethylamino)quinoxaline (IR (KBr): 3347, 2936, 1580, 1523, 1129 cm^{-1}). 4.5 g of this product are then treated with 20 ml of 48% HBr and the mixture is refluxed

for 4 h. After cooling down, the mixture is neutralized with aqueous NaOH and the resulting precipitate is filtered under vacuum and dried to obtain 3.2 g of imidazo[1,2-a]quinoxalin-4(5H)-one (m.p. >300°C)

(b) A mixture of 0.47 g of imidazo[1,2-a]quinoxalin-4(5H)-one and 0.42 ml of N,N-dimethylaniline in 5.6 ml of phosphorus oxychloride is refluxed for 2 h. After evaporating under vacuum the resulting mixture, the residue is taken up in chloroform and repeatedly washed with water, then with saturated NaCl, then it is dried and evaporated thereby obtaining, after recrystallization from n-hexane / chloroform, 0.29 g of 4-chloroimidazo-[1,2-a]quinoxaline (IR (KBr): 1456, 755 cm^{-1}).

(c) A mixture of 0.25 g of 4-chloromidazo[1,2-α]quinoxaline and 0.5 ml of hydrazine hydrate in 1.5 ml of ethanol is refluxed for 2 h. After cooling the mixture, the resulting precipitate is filtered under vacuum, washed and dried, thereby obtaining 0.22 g of 4-hydrazinoimidazo[1,2-a]quinoxaline (IR (KBr): 3308, 3237, 1570 cm^{-1}).

(d) A mixture of 0.17 g of 4-hydrazinoimidazo[1,2-a]quinoxaline and 3.4 ml of Raney nickel in 20 ml of water is refluxed for 1.5 h. After cooling down, the mixture is filtered on Celite, followed by washing with methanolic chloroform. The filtrate is concentrated under vacuum and extracted with ethyl acetate. The organic extracts are then washed with saturated NaCl, dried and evaporated, thereby obtaining 0.17 g of imidazo[1,2-a]quinoxalin-4-amine. M.p. (DSC) = 205.3°C (onset); IR

(KBr): 3301, 3143, 1653, 1525 cm^{-1}; ^1H-NMR ($CDCl_3$): δ 8.0 (1H,s), 7.8÷7.45 (3H,m), 7.45÷7.2 (2H,m), 5.8 (2H,sb) ; UV (EtOH): λ_{max}= 229, 295, 331 nm. Elementary analysis for $C_{10}H_8N_4$ (m.w. 184.20): calcd. C 65.21, H 4.38, N 30.42%; found C 65.48, H 4.71, N 30.10%.

Example 2

(a) A mixture of 10 g of 2,3-dichloroquinoxaline, 4.5 ml of propargylamine, 10.5 ml of triethylamine in 50 ml of ethanol is refluxed for 4 h. After evaporating under vacuum the resulting mixture, the residue is chromatographed on SiO_2 (eluent: CH_2Cl_2) thereby obtaining 7.0 g of 2-chloro-3-(propargylamino)quinoxaline (IR (KBr) : 3441, 3282, 1518 cm^{-1}). This product is then added with 10 ml of concentrated sulphuric acid and the resulting mixture is stirred at 90°C for 1 h. After cooling down and cautiously neutralizing with aqueous NaOH, the resulting precipitate is filtered under vacuum, washed, dried, decolorized and recrystallized from dimethylformamide, thereby obtaining 2.4 g of 1-methylimidazo[1,2-a]quinoxaline-4(5H)-one (m.p. >300°C).

(b) The chlorination of 1-methylimidazo[1,2-a]quinoxalin-4(5H)-one with $POCl_3$ is carried out according to a closely analogous procedure to that reported in example 1 (b), thereby obtaining 4-chloro-1-methylimidazo[1,2-a]quinoxaline (IR (KBr): 1486, 754 cm^{-1}).

(c) The reaction of 4-chloro-1-methylimidazo[1,2-a]quinoxaline with hydrazine hydrate is carried out

according to a strictly analogous procedure to that followed in example 1 (c), thereby obtaining 4-hydrazino-1-methylimidazo[1,2-a]quinoxaline (IR (KBr): 3298, 3250, 1564 cm^{-1}).

(d) The hydrogenation of 4-hydrazino-1-methylimidazo[1,2-a]quinoxaline with Raney nickel is carried out according to a strictly analogous procedure to that followed in example 1 (d), thereby obtaining 1-methylimidazo[1,2-a]quinoxalin-4-amine. m.p. (DSC) = 184.8°C (onset); IR (KBr): 3379, 3295, 1640, 1516 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 8.05 (1H,dd), 7.9÷7.2 (3H,m), 7.2 (1H,s), 5,7 (2H, sb), 2.85 (3H, s) ; UV (EtOH): λ_{max}= 225, 270, 304, 329 nm. Elementary analysis for $C_{11}H_{10}N_4$ (m.w. 198.23):

calcd. C 66.65, H 5.08, N 28.26%;

found C 66.79, H 5.30, N 28.03%.

Example 3

A mixture of 2,8 g of 4-chloroimidazo[1,2-a]quinoxaline (example 1) and 9.8 ml of diethylamine in 40 ml of ethanol is refluxed for 4 h. After evaporating the solvent, the residue is taken up in chloroform and washed with water and saturated NaCl, then dried and evaporated, thereby obtaining 2.2 g of raw product that is subsequently chromatographed on SiO_2 (eluent: CH_2Cl_2): after recrystallization from n-hexane there are obtained 1.3 g of 4- diethylaminoimidazo[1,2-a]quinoxaline. m.p. (DSC) = 91.7°C (onset); IR (KBr):

2976, 1518, 1425, cm^{-1} ; ^{1}H-NMR ($CDCl_3$): δ 7.9 (1H,s), 7.7÷7.4 (3H,m), 7.35÷7.05 (2H,m), 4.15 (4H,q), 1.3

(6H,t); UV (EtOH): λ_{max}= 231, 250, 293, 305, 332, 348 nm.

Elementary analysis for $C_{14}H_{16}N_4$ (m.w. 240.31):

calcd. C 69.97, H 6.71, N 23.31%;

found C 69.99, H 6.80, N 23.13%.

<u>Example 4</u>

By reaction of 4-chloroimidazo[1,2-a]quinoxaline (example 1) with isopropylamine according to a procedure that is similar to that followed in example 3 there is obtained 4-isopropylaminoimidazo[1,2-a]quinoxaline. m.p. (DSC) = 102.7°C (onset); IR (KBr): 3230, 2966, 1559 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 8.55 (1H,s), 8.2÷7.95 (1H,m), 7.6÷7.4 (2H,m), 7.4÷7.2 (3H,m), 4.5 (1H,m), 1.25 (6H,d) ; UV (EtOH): λ_{max}= 227, 244, 285, 297, 318, 332 nm.

Elementary analysis for $C_{13}H_{14}N_4$ (m.w. 226.28):

calcd. C 69.00, H 6.23, N 24.76%;

found C 69.17, H 6.70, N 25.05%.

<u>Example 5</u>

By reaction of 4-chloro-1-methylimidazo[1,2-a]quinoxaline (example 2) with 1-ethylpropylamine, according to a procedure that is similar to that followed in example 3, there is obtained 4-(1-ethylpropylamino)-1-methylimidazo[1,2-a] quinoxaline. m.p. (DSC) = 75.9°C (onset); IR (KBr): 3231, 2965, 1546 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 8.0 (1H,dd), 7.7 (1H,dd), 7.4÷7.1 (3H,m), 5.9 (1H,d), 4.2 (1H,m), 2.85 (3H,s), 1.65 (4H,m), 0.95 (6H,t) ; UV (EtOH): λ_{max}= 221, 241, 268, 298, 313 nm.

Elementary analysis for $C_{16}H_{20}N_4$ (m.w. 268.36):

calcd. C 71.61, H 7.51, N 20.83%;

found C 71.12, H 7.53, N 20.79%.

Example 6

By reaction of 4-chloromidazo[1,2-a]quinoxaline (example 1) with ethanolamine according to a procedure that is similar to that followed in example 3 there is obtained 4-(2-hydroxyethylamino)imidazo[1,2-a] quinoxaline. m.p. (DSC) = 150.8°C (onset); IR (KBr): 3312, 1598, 1564 cm^{-1};

^{1}H-NMR ($CDCl_3$/CD_3OD): δ 8.2 (1H,s), 8.1÷7.55 (2H,m), 7.55 (1H,s), 7.4÷7.2 (2H,m), 3.8 (4H,s) ; UV (EtOH): λ_{max}= 227, 285, 297, 317, 330 nm.

Elementary analysis for $C_{12}H_{12}N_4$ (m.w. 228.25):

calcd. C 63.14, H 5.30, N 24.55%;

found C 63.16, H 5.40, N 24.99%.

Example 7

By reaction of 4-chloro-1-methylimidazo[1,2-a]quinoxaline (example 2) with ethanolamine, according to a procedure that is similar to that followed in example 3 there is obtained 4-(2-hydroxyethylamino)-1-methyl imidazo[1,2-a]quinoxaline. m.p. (DSC) = 173.4°C (onset); IR (KBr): 3415, 3217, 1558 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 8.0 (1H,dd), 7.7÷7.2 (3H,m), 7.2 (1H,s), 6.6 (1H,m), 5.3 (1H,sb), 3.85 (4H,m), 2.8 (3H,s) ; UV (EtOH): λ_{max}= 225, 242, 271, 301, 314, 327 nm.

Elementary analysis for $C_{13}H_{14}N_4$ (m.w. 242.28):

calcd. C 64.45, H 5.82, N 23.12%;

found C 64.29, H 5.91, N 23.13%.

Example 8

By reaction of 4-chloromidazo[1,2-a]quinoxaline

(example 1) with cyclopentylamine according to a procedure that is similar to that followed in example 3 there is obtained 4-cyclopentylaminoimidazo[1,2-a] quinoxaline. m.p. (DSC) = 114.3°C (onset); IR (KBr): 3419, 2962, 1543 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 7.9 (1H,s), 7.8÷7.0 (5H,m), 6.2 (1H,d), 4.7 (1H,m), 2.3÷2.05 (4H,m), 2.0÷1.3 (4H,m); UV (EtOH): λ_{max}= 228, 244, 285, 297, 319, 333 nm.

Elementary analysis for $C_{15}H_{16}N_4$ (m.w. 252.32):
calcd. C 71.40, H 6.39, N 22.20%;
found C 71.13, H 7.30, N 22.29%.

Example 9

A mixture of 3.5 g of 1-methylimidazo[1,2-a] quinoxalin-4(5H)-one (example 2), 13 ml of hexamethyl disilazane, 0.5 g of ammonium sulphate and 8.7 ml di cyclopentylamine is stirred at 120°C in a Dean-Stark apparatus for 24 h. After concentrating the resulting mixture under vacuum, the residue is added with water and extracted with ethyl acetate. The organic extracts are then washed with water and saturated NaCl, dried and evaporated, thereby obtaining 1.5 g of a raw product that is subsequently chromatographed on SiO_2 (eluent: CH_2Cl_2/AcOEt 97:3). By recrystallizing from ethyl acetate, there is obtained 4-cyclopentylamino-1-methyl imidazo [1,2-a]quinoxaline.

m.p. (DSC) = 167.3°C (onset); IR (KBr): 3294, 2948, 1544 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 8.0 (1H,dd), 7.7 (1H,dd), 7.4÷7.05 (3H,m), 6.0 (1H,d), 4.6 (1H,m), 2.8 (3H,s), 2.3÷2.05 (4H,m), 2.0÷1.4 (4H,m); UV (EtOH): λ_{max}= 225, 243, 272,

301, 316, 329 nm.

Elementary analysis for $C_{16}H_{18}N_4$ (m.w. 266.35):

calcd. C 72.15, H 6.81, N 21.03%;

found C 71.86, H 6.81, N 20.79%.

Example 10

By reaction of 4-chloroimidazo[1,2-a]quinoxaline (example 1) with cylohexylamine, according to a procedure that is similar to that followed in example 3, there is obtained 4-cyclohexylaminoimidazo[1,2-a]quinoxaline. m.p. (DSC)= 94.0°C (onset); IR (KBr): 3227, 2924, 1560 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 7.85 (1H,d, J=2Hz), 7.8÷7.4 (3H,m), 7.4÷7.1 (2H,m), 6.0 (1H,d), 4.2 (1H,m), 2.3÷1.95 (4H,m), 1.95÷0.9 (6H,m) ; UV (EtOH): λ_{max}= 225, 242, 283, 294, 316, 330 nm.

Elementary analysis for $C_{16}H_{18}N_4$ (m.w.266.35):

calcd. C 72.15, H 6.81, N 21.03%;

found C 72.25, H 7.04, N 21.19%.

Example 11

By reaction of 1-methylimidazo[1,2-a]quinoxalin-4(5H)-one (example 2) with cyclohexylamine, according to a procedure that is similar to that followed in example 9, there is obtained 4-cyclohexylamino-1-methyl imidazo [1,2-a]quinoxaline. m.p. (DSC)=126.5°C (onset); IR (KBr): 3345, 2938, 1546 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 8.0 (1H,dd), 7.7 (1H,dd), 7.5÷7.1 (3H,m), 6.0 (1H,d), 4.2 (1H,m), 2.85 (3H,s), 2.3÷1.95 (4H,m), 1.95÷0.9 (6H,m); UV (EtOH): λ_{max} = 225, 243, 272, 301, 316, 329 nm.

Elementary analysis for $C_{17}H_{20}N_4$ (m.w. 280.37):

calcd. C 72.83, H 7.19, N 19.98%;

found C 72.21, H 7.54, N 20.14%.

Example 12

By reaction of 4-chloroimidazo[1,2-a]quinoxaline (example 1) with piperidine, according to a procedure that is similar to that followed in example 3, there is obtained 4-(1-piperidinyl)imidazo[1,2-a]quinoxaline. m.p. (DSC)=108.2°C(onset); IR(KBr): 3107, 2935, 1517 cm^{-1}; ^1H-NMR ($CDCl_3$): δ7.9 (1H,d, J=2Hz), 7.75÷7.4 (3H,m), 7.4÷7.1 (2H,m), 4.3 (4H,t), 1.9÷1.6 (6H,m); UV (EtOH): λ_{max}= 231, 249, 293, 305, 333 nm.

Elementary analysis for $C_{15}H_{16}N_4$ (m.w. 252.32):

calcd. C 71.40, H 6.39, N 22.20%;

found C 71.38, H 6.63, N 22.61%.

Example 13

By reaction of 4-chloro-1-methylimidazo[1,2-a]quinoxaline (example 2) with piperidine, according to a procedure that is similar to that followed in example 3, there is obtained 1-methyl-4-piperidinylimidazo[1,2-a]quinoxaline. m.p. (DSC) = 78.9°C (onset); IR (KBr): 3018, 2927, 1502 cm^{-1}; ^1H-NMR ($CDCl_3$): δ8.05 (1H,dd), 7.65 (1H,dd), 7.5÷7.0 (3H,m), 4.25 (4H,t), 2.85 (3H,s), 1.9÷1.6 (6H,m); UV (EtOH): λ_{max}= 249, 281, 297, 310, 329 nm.

Elementary analysis for $C_{16}H_{18}N_4$ (m.w. 266.35):

calcd. C 72.15, H 6.81, N 21.03%;

found C 71.84, H 7.09, N 20.70%.

Example 14

By reaction of 4-chloroimidazo[1,2-a]quinoxaline (example 1) with morpholine, according to a procedure

that is similar to that followed in example 3, there is obtained 4-(4-morpholinyl)imidazo[1,2-a]quinoxaline. m.p. (DSC)= 142.8°C (onset); IR (KBr): 3016, 2962, 1517 cm^{-1}; ^1H-NMR ($CDCl_3$): δ 8.0 (1H,s), 7.8÷7.5 (3H,m), 7.5÷7.2 (2H,m), 4.4 (4H,t), 3.9 (4H,t); UV (EtOH): λ_{max}= 230, 248, 292, 304, 330 nm.

Elementary analysis for $C_{14}H_{14}N_4O$ (m.w. 254.29):

calcd. C 66.13, H 5.55, N 22.03%;

found C 65.43, H 5.47, N 22.25%.

Example 15

By reaction of 4-chloroimidazo[1,2-a]quinoxaline (example 1) with N-methylpiperazine, according to a procedure that is similar to that followed in example 3, there is obtained 4-(N'-methylpiperazinyl)imidazo[1,2-a] quinoxaline, that is subsequently converted to the dihydrochloride by treatment with ethanolic HCl. m.p. (DSC)= 305.6°c (onset); IR (KBr): 2697, 1560, 1508 cm^{-1}; ^1H-NMR (DMSO-d_6/CD_3OD): δ 8.7 (1H,sb), 8.3÷8.0 (1H,m), 7.8÷7.35 (4H,m), 5.5 (4H,t), 3.7÷3.3 (4H,m), 2.8 (3H,s); UV (EtOH): λ_{max}= 230, 291, 304, 320 nm.

Elementary analysis for $C_{15}H_{17}N_5$.2HCl (m.w. 340.25):

calcd. C 52.95, H 5.63, N 20.58%;

found C 52.81, H 5.78, N 20.13%.

Example 16

By reaction of 4-chloro-1-methylimidazo[1,2-a]quinoxaline (example 2) with N-methylpiperazine, according to a procedure that is similar to that followed in example 3, there is obtained 1-methyl-4-(N'-methylpiperazinyl)imidazo[1,2-a]quinoxaline. m.p.

(DSC)= 108.0°C (onset); IR (KBr): 2928, 1535, 1510 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 8.1 (1H,dd), 7.7 (1H,dd), 7.4÷7.0 (3H,m), 4.35 (4H,t), 2.85 (3H,s), 2.6 (4H,t), 2.3 (3H,s); UV (EtOH): λ_{max}= 228, 248, 279, 309, 325 nm.

Elementary analysis for $C_{16}H_{19}N_5$ (m.w. 281.36):
calcd. C 68.30, H 6.81, N 24.89%;
found C 68.37, H 7.15, N 25.05%.

Example 17

By reaction of 2,3,6-trichloroquinoxaline with aminoacetaldehyde dimethyl acetal, according to a procedure that is similar to that described in example 1, there is obtained 8-chloroimidazo[1,2-a]quinoxalin-4(5H)-one (m.p.>300°C). By reacting this product with 1-ethyl propylamine according to the method described in example 9, there is obtained 8-chloro-4-(1-ethylpropyl-amino)imidazo[1,2-a]quinoxaline. m.p. (DSC)= 125.1°C (onset); IR (KBr) : 3406, 3105, 2964, 1532 cm^{-1}; ^{1}H-NMR ($CDCl_3/CD_3OD$): δ 8.4 (1H,s), 8.05 (1H,d, J=2Hz), 7.8÷7.4 (3H,m), 3.85 (1H,m), 1.65 (4H,m), 0.95 (6H,t); UV (EtOH): λ_{max}= 230, 245, 289, 301, 326 nm.

Elementary analysis for $C_{15}H_{17}ClN_4$ (m.w. 288.78):
calcd. C 62.39, H 5.93, N 19.40%;
found C 62.17, H 6.02, N 19.46%.

Example 18

By reacting 8-chloroimidazo[1,2-a]quinoxalin-4(5H)-one (example 17) with $POCl_3$, following a procedure that is similar to that described in example 1, there is obtained 4,8-dichloroimidazo[1,2-a]quinoxaline that is subsequently reacted with cyclopentylamine according to

the method described in example 3, thereby obtaining 4-cyclopentylamino-8-chloroimidazo[1,2-a]quinoxaline. m.p. (DSC) = 140.1°C (onset); IR (KBr): 3401, 2955, 1554 cm^{-1}; ^1H-NMR ($CDCl_3$): δ 7.8 (1H,d, J=2Hz), 7.7÷7.2 (4H,m), 6.15 (1H,d) 4.6 (1H,m), 2.3÷2.05 (4H,m), 2.05÷1.3 (4H,m); UV (EtOH): λ_{max}= 229, 245, 289, 301, 326, 340 nm.

Elementary analysis for $C_{15}H_{15}ClN_4$ (m.w. 286.76):

calcd. C 62.83, H 5.27, N 19.54%;

found C 63.04, H 5.36, N 19.64%.

Example 19

By reacting 4,8-dichloroimidazo[1,2-a]quinoxaline (example 18) with cyclohexylamine, following a procedure that is similar to that described in example 3, there is obtained 4-cyclohexylamino-8-chloroimidazo[1,2-a]quinoxaline. m.p. (DSC)=126.7°C (onset); IR (KBr): 3413, 2926, 1555 cm^{-1}; ^1H-NMR ($CDCl_3$): δ 7.85 (1H,s), 7.7÷7.2 (4H,m), 6.1 (1H,d), 4.2 (1H,m), 2.3÷2.0 (4H,m), 2.0÷1.2 (6H,m); UV (EtOH): λ_{max}= 229, 245, 289, 301, 326, 340 nm.

Elementary analysis for $C_{16}H_{17}ClN_4$ (m.w. 300.79):

calcd. C 63.89, H 5.70, N 18.63%

found C 64.07, H 5.79, N 18.80%

Example 20

By reacting 2,3,6-trichloroquinoxaline with propargylamine, following a procedure that is similar to that described in example 2, there is obtained 8-chloro-1-methylimidazo[1,2-a]quinoxalin-4(5H)-one (m.p.>300°C) and, subsequently, 4,8-dichloro-1-methylimidazo[1,2-a]

quinoxaline. By reacting this product with cyclopentylamine according to the method described in example 3, there is obtained 4-cyclopentylamino-8-chloro-1-methylimidazo[1,2-a]quinoxaline. m.p. (DSC)= 130.5°C (onset); IR (KBr): 3421, 2954, 1555 cm^{-1}; ^1H-NMR ($CDCl_3$): δ 7.95 (1H,d, J=2Hz), 7.6 (1H,d, J=9Hz), 7.35÷7.15 (2H,m), 6.1 (1H,d), 4.5 (1H,s), 2.8 (3H,s), 2.4÷2.05 (4H,m), 2.0÷1.3 (4H,m); UV (EtOH): λ_{max}= 227, 251, 276, 305, 323, 336 nm.

Elementary analysis for $C_{16}H_{17}ClN_4$ (m.w. 300.79):

calcd. C 63.89, H 5.70, N 18.63%

found C 63.79, H 5.79, N 18.58%

Example 21

By reacting 4,8-dichloro-1-methylimidazo[1,2-a] quinoxaline (example 20) with cyclohexylamine, following a procedure that is similar to that described in example 3, there is obtained 4-cyclohexylamino-8-chloro-1-methylimidazo[1,2-a]quinoxaline. m.p. (DSC) = 130.4°C (onset); IR (KBr): 3410, 2927, 1551 cm^{-1}; ^1H-NMR ($CDCl_3$): δ 7.95 (1H,d, J=2Hz), 7.6 (1H,d, J=9Hz), 7.4÷7.2 (2H,m), 6.1 (1H,d), 4.2 (1H,m), 2.8 (3H,2), 2.3÷1.1 (10H,m); UV (EtOH): λ_{max}= 227, 250, 276, 305, 323, 336 nm.

Elementary analysis for $C_{17}H_{19}ClN_4$ (m.w. 314.82):

calcd. C 64.86, H 6.08, N 17.80%

found C 64.86, H 6.21, N 17.91%

Example 22

By reacting 2,3,6,7-tetrachloroquinoxaline with aminoacetaldehyde dimethyl acetal, following a procedure

that is similar to that described in example 1, there is obtained 7,8-dichloroimidazo[1,2-a]quinoxalin-4(5H)-one (m.p.>300°C) and, subsequently, 4,7,8-trichloroimidazo [1,2-a]quinoxaline. By reacting this product with cyclopentylamine according to the method described in example 3, there is obtained 4-cyclopentylamino-7,8-dichloroimidazo[1,2-a]quinoxaline.

m.p. (DSC) = 139.4°C (onset); IR (KBr): 3247, 2961, 1589, 1556 cm^{-1} ; ^{1}H-NMR ($CDCl_3$): δ 7.8 (2H,m), 7.7 (1H,s), 7.55 (1H,s), 6.2 (1H,d), 4.6 (1H,m), 2.4÷1.3 (8H,m); UV (EtOH): λ_{max}= 235, 274, 292, 304, 330, 345 nm.

Elementary analysis for $C_{15}H_{14}Cl_2N_4$ (m.w. 321.21):

calcd. C 56.09, H 4.39, N 17.44%;

found C 56.13, H 4.41, N 17.52%.

Example 23

By reacting 4,7,8-trichloroimidazo[1,2-a]quinoxaline (example 22) with cyclohexylamine, following a procedure that is similar to that described in example 3, there is obtained 4-cyclohexylamino-7,8-dichloroimidazo[1,2-a] quinoxaline. m.p. (DSC) = 162.3°C (onset); IR (KBr): 3332, 2929, 1587, 1550 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 7.8 (2H,m), 7.7 (1H,s), 7.55 (1H,d, J=2Hz), 6.2 (1H,d), 4.4 (1H,m), 2.3÷1.2 (10H,m); UV (EtOH): λ_{max}= 234, 274, 292, 304, 330, 345 nm.

Elementary analysis for $C_{16}H_{16}Cl_2N_4$.1/2H_2O (m.w. 344.25):

calcd. C 55.82, H 4.98, N 16.28%

found C 55.83, H 5.00, N 16.31%

Example 24

By reacting 2,3,6,7-tetrachloroquinoxaline with

propargylamine, following a procedure that is similar to that described in example 2 there is obtained 7,8-dichloro-1-methylimidazo[1,2-a]quinoxalin-4(5H)-one (m.p.>300°C) and, subsequently, 1-methyl-4,7,8-trichloro-imidazo[1,2-a]quinoxaline. By reacting this product with cyclopentylamine according to the method described in example 3, there is obtained 4-cyclopentylamino-7,8-dichloro-1-methylimidazo[1,2-a]quinoxaline.

m.p. (DSC) = 213.5°C (onset); IR (KBr): 3411, 2960, 1548 cm^{-1}; ^1H-NMR ($CDCl_3$): δ 8.0 (1H,s), 7.75 (1H,s), 7.25 (1H,s), 6.2 (1H,d), 4.6 (1H,m), 2.8 (3H,s), 2.3÷1.3 (8H,m); UV (EtOH): λ_{max}= 233, 279, 308, 327, 341 nm.

Elementary analysis for $C_{16}H_{16}Cl_2N_4$ (m.w. 335.23):

calcd. C 57.33, H 4.81, N 16.71%;

found C 57.41, H 4.82, N 16.68%.

Example 25

By reacting 2,3-dichloro-6-fluoroquinoxaline with aminoacetaldehyde dimethyl acetal, following a procedure that is similar to that described in example 1, there is obtained 8-fluoroimidazo[1,2-a]quinoxalin-4(5H)-one (m.p. >300°C) and, subsequently, 4-chloro-8-fluoroimidazo[1,2-a]quinoxaline. By reacting this product with cyclopentyl amine according to the method described in example 3, there is obtained 4-cyclopentylamino-8-fluoroimidazo[1,2-a]quinoxaline.

m.p. (DSC) = 85.7°C (onset); IR (KBr) : 3255, 2964, 1551 cm^{-1}; ^1H-NMR ($CDCl_3$): δ 7.8 (1H,s), 7.7÷7.35 (1H,dd, J_{HF}=16Hz), 7.5 (1H,d, J=2Hz), 7.6÷7.25 (1H,dd, J_{HF}=16Hz), 7.05 (1H,dd), 6.0 (1H,d), 4.55 (1H,m), 2.35÷1.3 (8H,m);

UV (EtOH): λ_{max}= 226, 268, 285, 296, 323, 336 nm.

Elementary analysis for $C_{15}H_{15}FN_4$ (m.w. 270.31):

calcd. C 66.65, H 5.59, N 20.73%;

found C 66.36, H 5.66, N 20.86%.

Example 26

By reacting 4-chloro-8-fluoroimidazo[1,2-a] quinoxaline (example 25) with cyclohexylamine, following a procedure that is similar to that described in example 3, there is obtained 4-cyclohexylamino-8-fluoro-imidazo[1,2-a]quinoxaline. m.p. (DSC) = 157.6°C (onset); IR (KBr): 3415, 2927, 1556 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 7.8 (1H,dd, J=2Hz), 7.7÷7.35 (1H,dd, J_{HF}=16Hz), 7.55 (1H,d, J=2Hz), 7.55÷7.25 (1H,dd, J_{HF}=16Hz), 7.05 (1H,dd), 6.0 (1H,d), 4.25 (1H,m), 2.35÷1.2 (10H,m); UV (EtOH): λ_{max}= 226, 239, 285, 297, 323, 337 nm.

Elementary analysis for $C_{16}H_{17}FN_4$ (m.w. 284.33):

calcd. C 67.59, H 6.03, N 19.71%

found C 67.31, H 6.04, N 19.70%

Example 27

By reacting 2,3-dichloro-6,7-difluoroquinoxaline with aminoacetaldehyde dimethyl acetal, following a procedure that is similar to that described in example 1, there is obtained 7,8-difluoroimidazo[1,2-a]quinoxalin-4(5H)-one (m.p. >300°C) and, subsequently, 4-chloro-7,8-difluoroimidazo[1,2-a]quinoxaline. By reacting this product with cyclopentylamine according to the method described in example 3, there is obtained 4-cyclo-pentylamino-7,8-difluoroimidazo[1,2-a]quinoxaline. m.p.

(DSC) = 146.0°C (onset); IR (KBr): 3263, 2955, 1554 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 7.7 (1H,s), 7.65÷7.15 (3H,m), 6.1 (1H,d), 4.6 (1H,m), 2.3÷1.3 (8H,m); UV (EtOH): λ_{max} = 225, 241, 270, 295, 323, 337 nm.

Elementary analysis for $C_{15}H_{14}F_2N_4$ (m.w. 288.30):
calcd. C 62.49, H 4.89, N 19.43%;
found C 62.46, H 5.03, N 19.65%.

Example 28

Binding on the adenosine receptors.

The binding on A_1 receptors has been carried out according to the method described in Naunyn-Schmied. Arch. Pharmacol. 1987, 336, 204 on preparations of synaptosomial membranes from rat brain by incubating 200 µg of membrane proteins for 1 h at 25°C with the substance to be tested and 0.3 nM [^{3}H]-DPCPX in 400 µl of 50 mM Tris.HCl pH = 7.4. The non-specific binding has been determined with 5 nM R-PIA.

The binding on A_2 receptors has been carried out according to the method described in FASEB J. 1989, 3, A1047 on preparations of rat striatal membranes by incubating 200 µg of membrane proteins for 1 h at 25°C with the substance to be tested, 5 nM [^{3}H]-CGS21680 and 50 nM CPA. The non-specific binding has been determined with 100 nM CPA.

The incubations were blocked by filtration by means of a cell-harvester and, after completion of the separation of the bound from the free, the radioactivity contents were evaluated by liquid scintillation. The concentration-inhibition curves were obtained by assaying

the receptor displacement at at least ten different concentrations of the test substance (all the assays were carried out in triplicate). The tested substances were dissolved in dimethyl sulphoxide and diluted in 50 mM Tris.HCl buffer pH = 7.4. The IC_{50} values have been determined by non-linear regression curves and transformed into Ki values according to the Cheng-Prusoff equation.

Table I shows the results obtained with the compounds of examples 5, 9, 13, 18, 22 and 25 of the invention.

TABLE I: Adenosine receptors affinities :

Substance	Ki, A_1 (nM)	Ki, A_2 (µM)
COMPOUND EX. 5	54	
COMPOUND EX. 9	7,9	2,5
COMPOUND EX. 13	-	2,6
COMPOUND EX. 18	23,5	
COMPOUND EX. 22	26,5	
COMPOUND EX. 25	84	

Example 29

Forced swim test

The test described by R.D.Porsolt et al. in Arch.Int.Pharmacodyn.Ther. 1977, 229, 327, has been carried out which is widely used as an animal model for the study of the antidepressant activity of new drugs. Male albino CD 1 mice weighing 25-35 g were used.

One hour before immersion in water, the test compound is intraperitoneally (i.p.) administered to the animal; the vehicle is administered to the control animals. The duration of permanence in water is 6': from the 2^{nd} to the 6^{th} minute the time is measured during which the animal remains motionless. Table II shows the results obtained with the compounds of examples 9, 13, 16, 18 and 21 of the invention, expressed as the percent variation of the immobility time of the treated animals versus the control group. As the reference substance the tricyclic antidepressant drug desipramine was used.

TABLE II: Forced swim test

Substance	Dose (mg/kg.i.p.)	%variation immobility time vs.C.
COMPOUND EX.9	0.001	-32.8***
COMPOUND EX.9	0.01	-45.3***
COMPOUND EX.13	0.1	-23.5*
COMPOUND EX.13	1	-70.7***
COMPOUND EX.16	0.1	-22.4
COMPOUND EX.16	1	-51.4***
COMPOUND EX.18	1	-42.3***
COMPOUND EX.18	10	-52.8***
COMPOUND EX.21	0.001	-33.0**
COMPOUND EX.21	0.01	-48.6***
DESIPRAMINE	7.5	-10.4**
DESIPRAMINE	30	-41.4***

(***) $p<0.001$; (**) $p<0.01$; (*) $p<0.05$

Example 30

Tail suspension test

The test described by L.Steru, et al. in Psychopharmacology 1985, 85, 367, also widely used as an animal model for the screening of antidepressant activity has been carried out.

Male albino CD 1 mice weighing 25-35 g were used.

Half an hour before the test, the animal is

administered the test compound by the i.p. route; the control animals are administered the vehicle. The mouse is suspended from a horizontal bar at about 40 cm from the support plane by means of an adhesive tape applied at the end of the tail and secured to a hook. The immobility time period is registered during 6'.

Table III shows the results obtained with the compound of example 9 of the invention, as the percent change of the immobility time period of the treated animals versus the control group.

As the reference substance the tricyclic antidepressant drug desipramine was used.

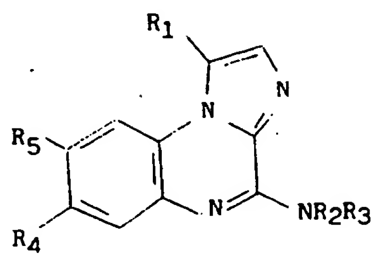
TABLE III: Tail suspension test

TABLE III: Tail suspension test		
Substance	Dose (mg/kg.i.p.)	%variation immobility time vs.C.
COMPOUND EX.9	0.001	-26.7
COMPOUND EX.9	0.01	-41.1*
COMPOUND EX.9	0.1	-64.3***
DESYPRAMINE	4	-21.3
DESYPRAMINE	16	-62.4**

(***) $p<0.001$; (**) $p<0.01$; (*) $p<0.05$

CLAIMS

1. A compound of the formula (I):



(I)

wherein:

R_1 is hydrogen or methyl;

R_2 is hydrogen, straight- or branched- chain (C_1-C_6)alkyl;

R_3 is hydrogen, straight- or branched- chain (C_1-C_8)alkyl that is possibly substituted with OH, (C_3-C_8)cycloalkyl;

or R_2 and R_3 together form

```
------(CH2)m
            \
             Z
            /
------(CH2)n
```

wherein Z is a direct bond, or O, NR_6, R_6 being a straight- or branched- chain (C_1-C_6)alkyl;

m and *n*, same or different, are 1, 2 or 3;

R_4 and R_5 can be the same or different and are hydrogen or halogen chosen from Cl, F, Br;

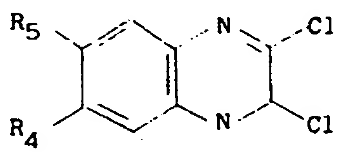
and its pharmacologically acceptable salts

2. A compound according to claim 1 characterized in that R_1 is hydrogen or methyl, R_2 is hydrogen, R_3 is hydrogen, straight- or branched- chain (C_1-C_6)alkyl that is possibly substituted with OH, (C_5-C_6)cycloalkyl, R_4 and R_5 can be the same or different and are hydrogen,

chlorine or fluorine.

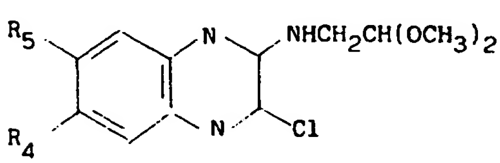
3. A compound according to claims 1 and 2 characterized in that R_1 is methyl, R_2 is hydrogen, R_3 is cyclopentyl, R_4 and R_5 are both hydrogen.

4. A process for the preparation of the compounds of the formula (I) according to claims 1 to 3, characterized in that a compound of formula (II)

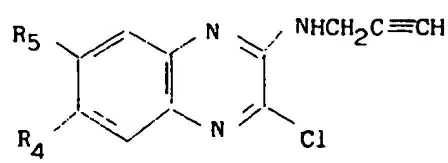


(II)

in which R_4 and R_5 are as defined in claim 1, is reacted with amino acetaldehyde dimethyl acetal or with propargyl amine, thereby to obtain, respectively, the compounds of the formulae (III) and (IV)

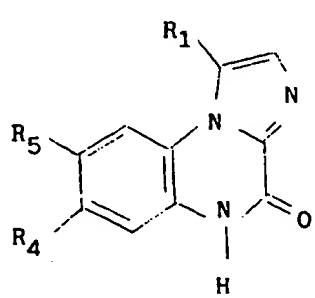


(III)



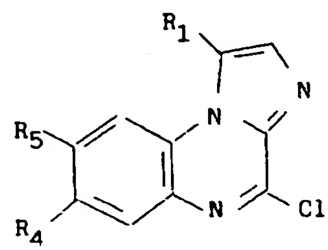
(IV)

in which R_4 and R_5 are as defined in claim 1, said compounds being subsequently cyclized in an acidic milieu to give the compound of formula (V)



(V)

in which R_1 is hydrogen or methyl, R_4 and R_5 are as defined in claim 1; compound (V) is then reacted with a chlorinating agent such as $POCl_3$ to provide the compound of formula (VI)



(VI)

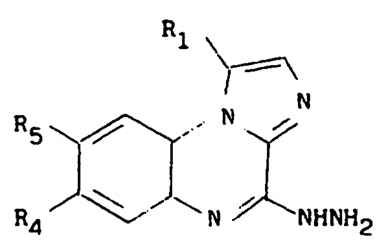
in which all the substituents are as defined above, which is subsequently reacted with the amine HNR_2R_3, in which R_2 and R_3 are as defined in claim 1;

or

compound (V), prepared as described above, is reacted with a silylating agent, such as hexamethyl disilazane, and amine HNR_2R_3, in which R_2 and R_3 are as defined in claim 1, at a temperature of between 80 and 180°C;

or

for the preparation of the compounds of formula (I) in which R_2 and R_3 are both hydrogen, the compound (VI), prepared as described above is reacted with hydrazine to give the compound of the formula (VII)



(VII)

in which R_1, R_4 and R_5 are as defined in claim 1, which is subsequently hydrogenated according to conventional methods.

5. Pharmaceutical compositions characterized in that they contain at least a compound according to claim 1 as an active ingredient at an effective dosage together with one or more conventional, non-toxic excipient.

6. Use of the compounds of claim 1 as adenosine antagonists.

7. Use of compounds according to claim 1 for the preparation of a medicament for the treatment of psychiatric disorders.

8. Use of compounds according to claim 1 for the preparation of a medicament for the treatment of neurological diseases of the central nervous system.

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/IB 96/01291

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D487/04 A61K31/505 //(C07D487/04,241:00,235:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 229 452 A (WARNER ET AL.) 21 October 1980 * See Table VII, columns 31-32, Compounds no. 167-169 * ---	1
X	CHEMICAL ABSTRACTS, vol. 77, no. 13, 25 September 1972 Columbus, Ohio, US; abstract no. 88433s, SIMONOV ET AL.: "Imidazo[1,2-a]quinoxaline and its reactions" page 457; XP002024866 & KHIM. GETEROTSIKL. SOEDIN, vol. 3, 1972, pages 416-418, see abstract ---	1
	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

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Date of the actual completion of the international search	Date of mailing of the international search report
10 February 1997	10.03.97

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

Inter al Application No
PCT/IB 96/01291

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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Y	US 4 780 464 A (TRIVEDI) 25 October 1988 see column 1 - column 5-8 ---	1
Y	JOURNAL OF MEDICINAL CHEMISTRY, vol. 34, no. 3, 1991, pages 1202-1206, XP002024865 P.J.M. VAN GALEN ET AL.: "1H-Imidazo[4,5-c]quinolin-4-amines: Novel Non-Xanthine Adenosine Antagonists" cited in the application see the whole document ---	1
A	US 5 182 386 A (ALBAUGH ET AL.) 26 January 1993 cited in the application see column 1-6 ---	1
A	WO 94 22865 A (BASF) 13 October 1994 cited in the application see page 1-2 -----	1

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Form PCT/ISA/210 (patent family annex) (July 1992)

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Information on patent family members

Inter ~al Application No
PCT/IB 96/01291

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		FI-A- 954614	28-09-95
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		JP-T- 8508271	03-09-96
		NO-A- 953892	29-09-95
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